IMPROVED INTERFERON POLYMER CONJUGATES

This application is a continuation-in-part of U.S. Patent Application Serial No. 08/337,567, filed November 10, 1994, which, in turn, is a continuation-in-part of U.S. Patent Application Serial No. 08/150,643, filed November 10, 1993, now abandoned. The contents of each application are incorporated herein by reference.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention is directed to interferon-polymer conjugates. In particular, the invention is directed to conjugates having a novel interferon-polymer attachment profile.

2. Description of Related Art

Conjugating biologically-active proteins to polymers has been suggested to improve one or more of the properties of circulating life, water solubility or antigenicity in vivo. For example, some of the initial concepts of coupling peptides or polypeptides to polyethylene glycol (PEG) and similar water-soluble polymers are disclosed in U.S. Patent No. 4,179,337, the disclosure of which is incorporated herein by reference.

Insulin and hemoglobin were among the first therapeutic agents conjugated. These relatively large polypeptides contain several free lysine ϵ-amino attachment sites. Several polymers could be attached without significant loss of biologic activity.

For many biologically active materials, the conjugation process, however, is not without complications. Care must be taken to limit the loss of biological activity caused by the conjugation reaction. For example, if too much of the activated polymer is attached to the target protein or polypeptide, biological activity can be severely reduced or lost. Further, if the wrong linker joining the polymer to the protein is used or an insufficient amount of polymer is attached to the target, the therapeutic value of the resultant conjugate is rather limited. Often, such conjugates do not demonstrate enough of an increase in the circulating life to compensate for the loss in bioactivity. Problems can also result when a therapeutic moiety's active site (i.e. where groups associated with bioactivity are found) becomes blocked as a result of the polymer attachment. This problem can be difficult to avoid since the polymer and protein are